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Fig. 1. Testicular ACE [2]. Ribbon model of tACE with an inhibitor, lisinopril, bound to the active site (space-filling red, blue and green atoms). The lid formed by helices α1 and α2 is indicated as a thin blue wire above the active site. The 7 evolutionarily conserved cysteines are indicated in yellow. The 2 cystines with their associated short β-sheets are visible. The cystine on the right of the figure links helix α17 to helix H7. The side wall formed by β4 and β5 is next to the active site, as indicated by lisinopril.

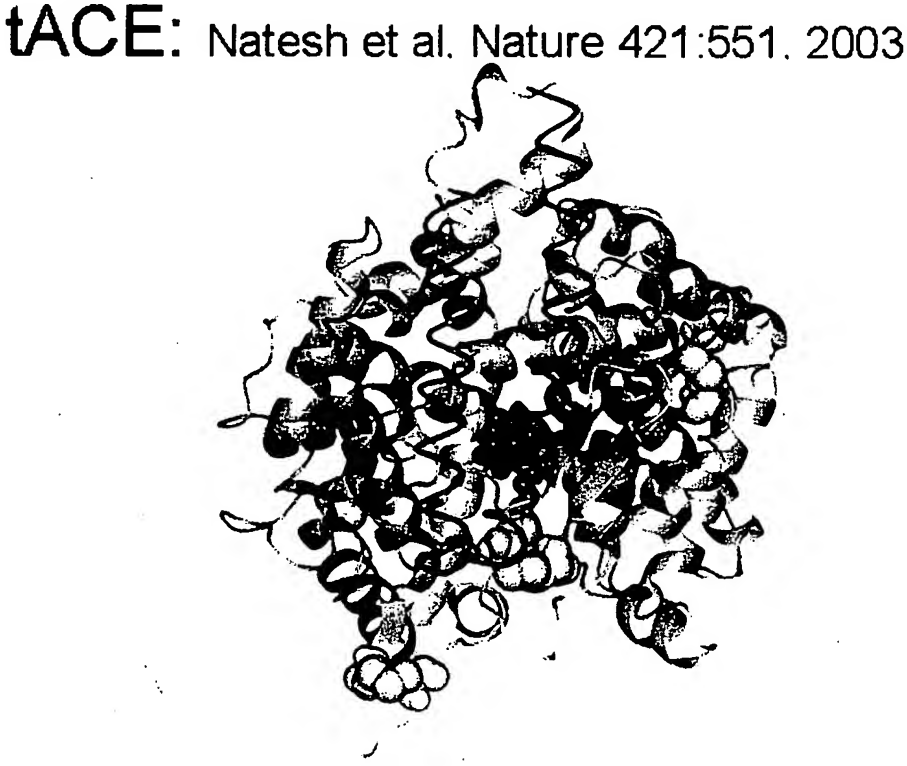
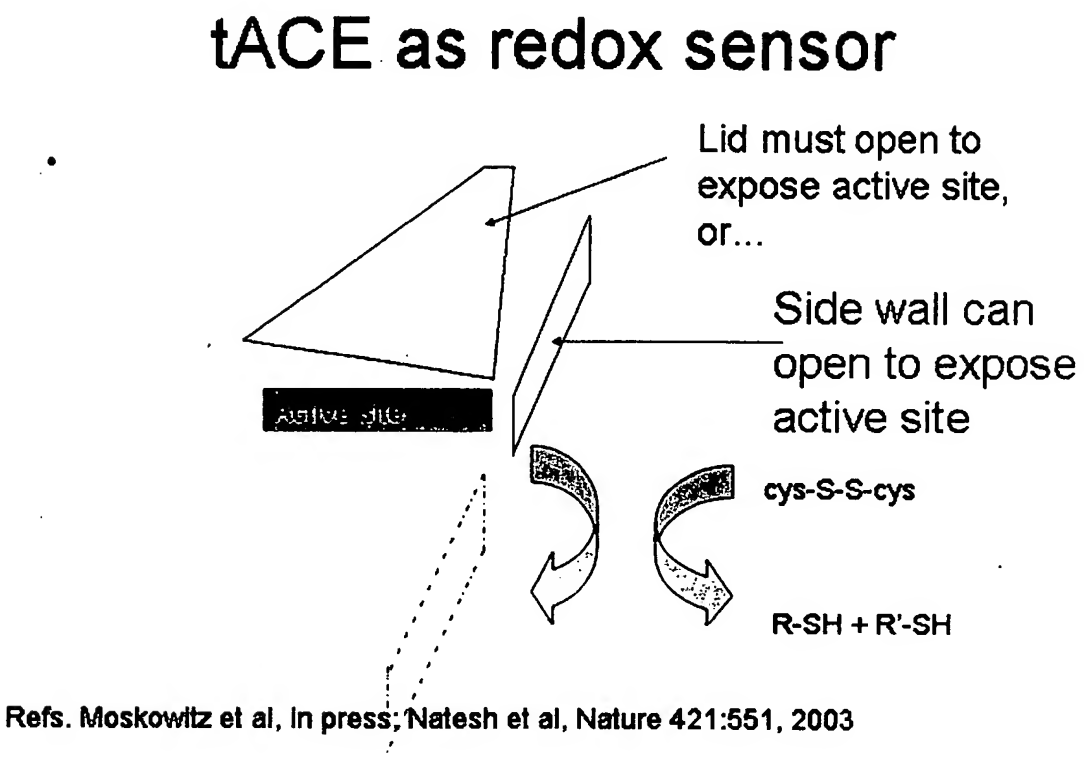


Fig. 2. Testicular ACE as redox- and mechanosensor.



Refs. Moskowitz et al, In press; Natesh et al, Nature 421:551, 2003

Fig. 3. *In silico* reduction of tACE: conversion of one cysteine to an alanine. "Reduction" of the middle cystine of tACE removes a side wall of the active site. C352 and C370 in this drawing correspond to C383 and C401, respectively, in the numbering scheme of the tACE precursor (SwissProt P22966).

Fig. 4a. Somatic ACE (sACE).

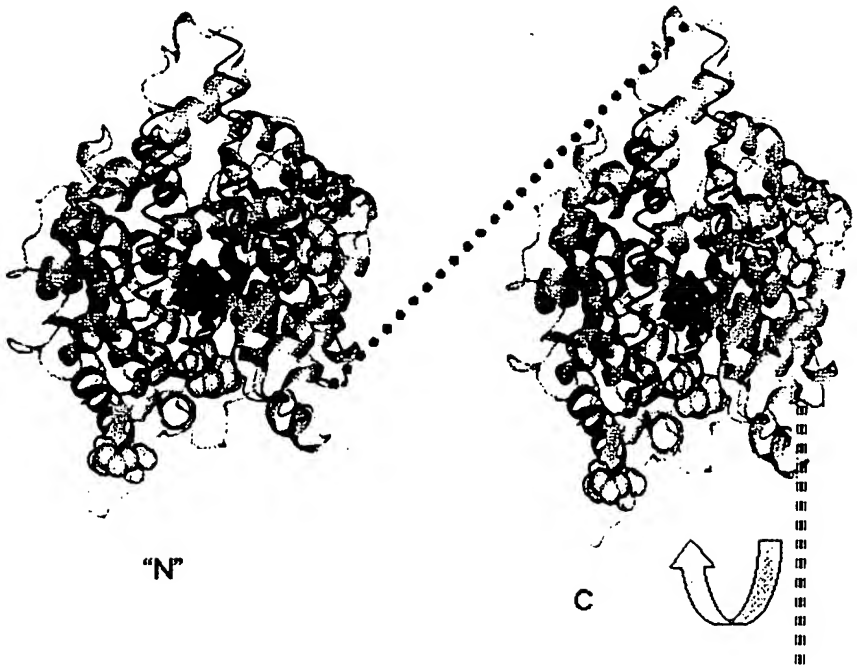


Fig. 4b. Somatic ACE showing complementarity of the N- and C-terminal domains. The secretase, an integral membrane protein associated with sACE, may have a chaperone-like function to hold the two domains of sACE together.

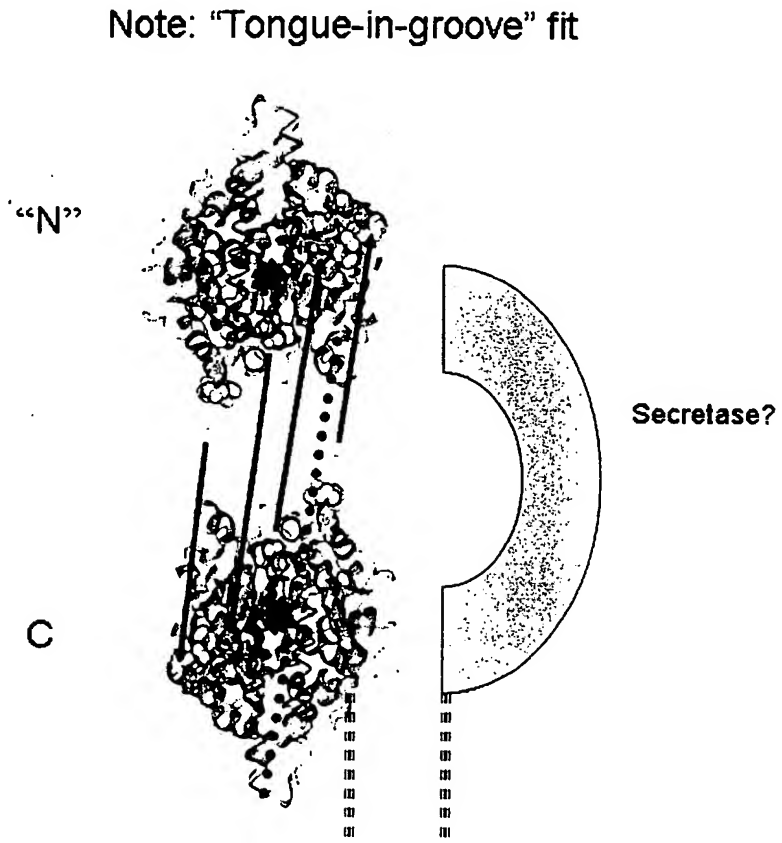


Figure 5. The "disulfide zipper" at the heart of sACE: a potential electron transport chain.

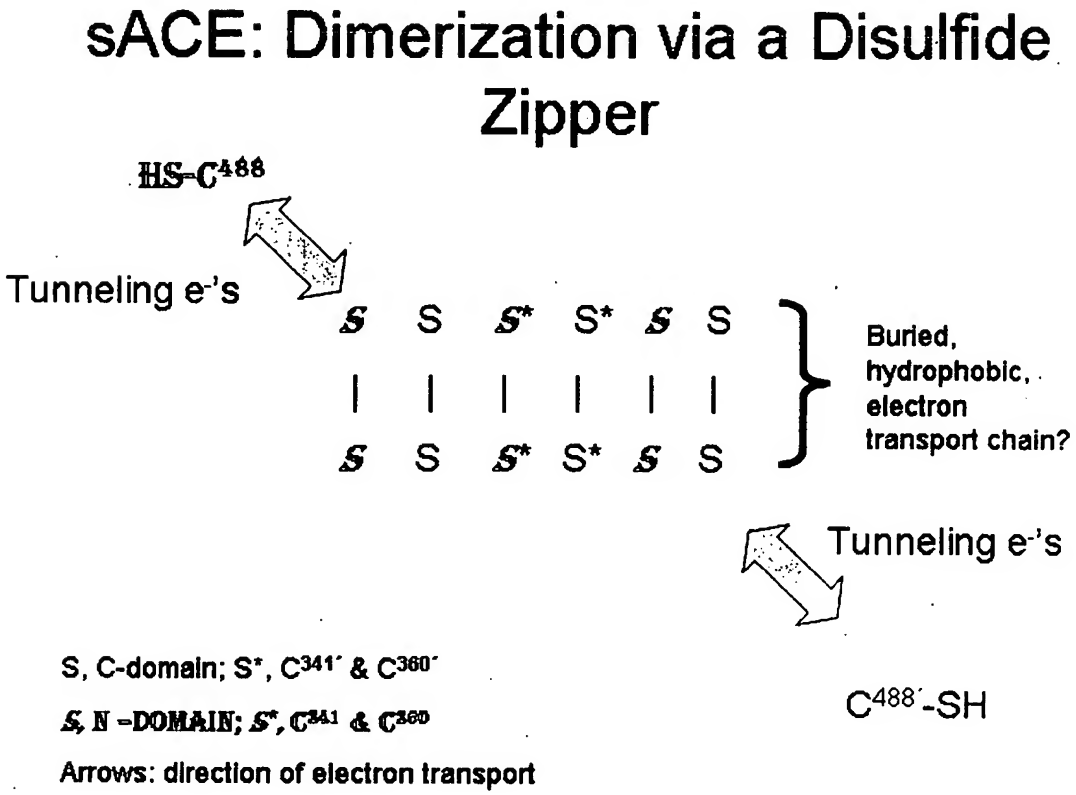


Figure 6. The disulfide isomerase exchange reaction possible at the heart of the disulfide zipper which might convert sACE into a kind of "reciprocating" enzyme.

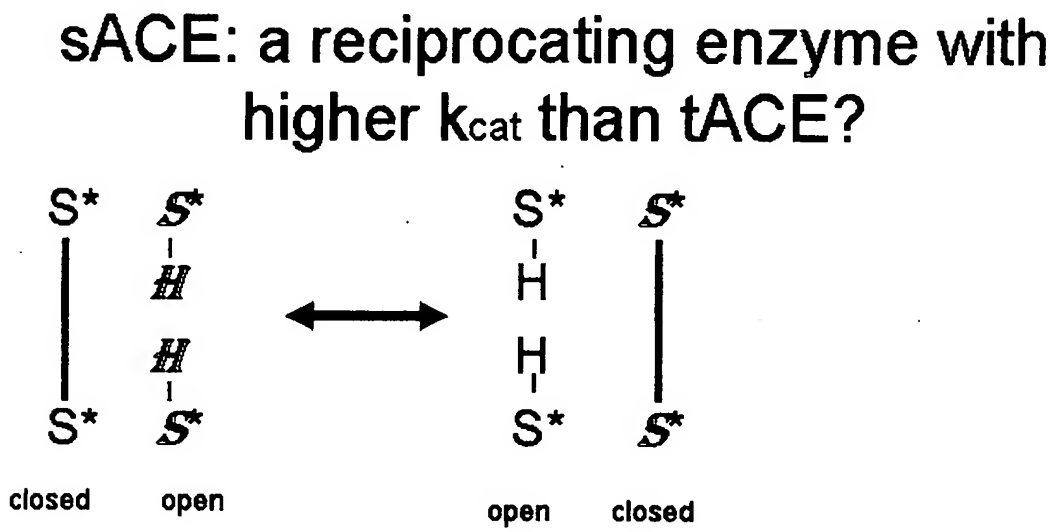


Figure 7. The two steps in the catalytic cycle of the "reciprocating" enzyme, sACE.

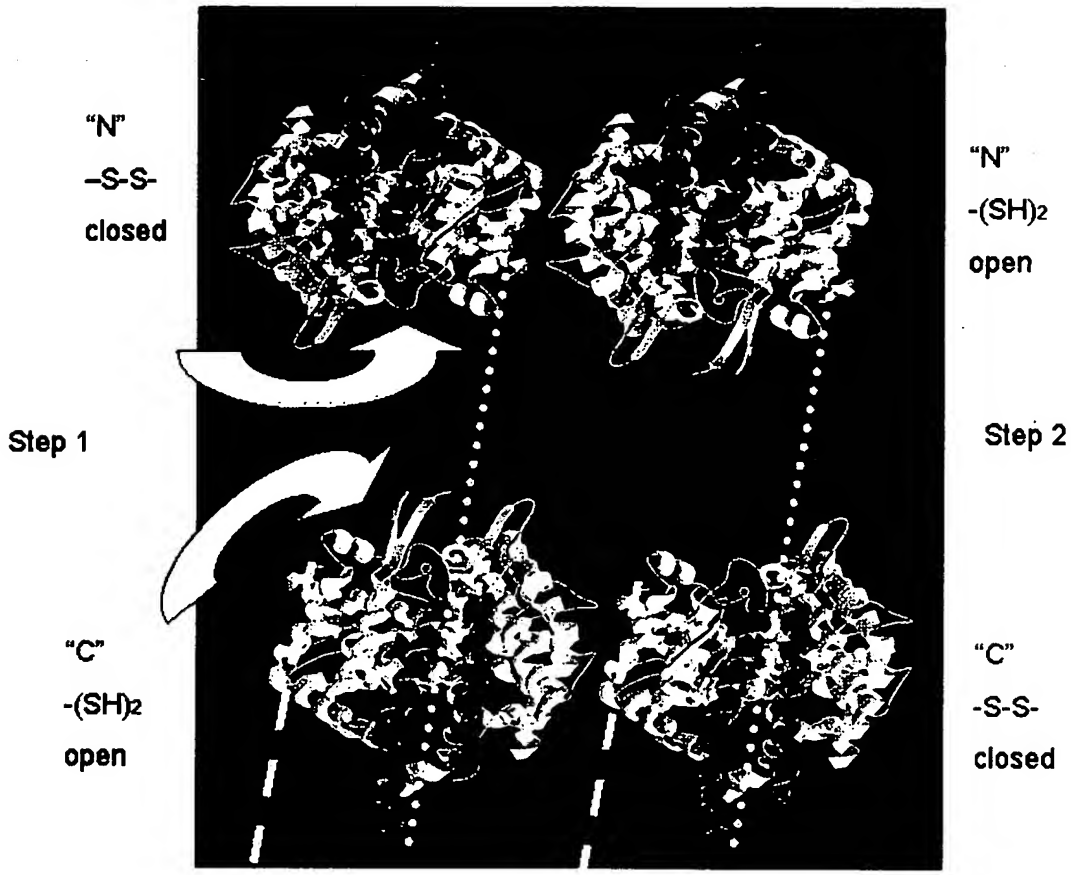


Figure 8. Pathway for transfer of NO from oxygenated hemoglobin to sACE.

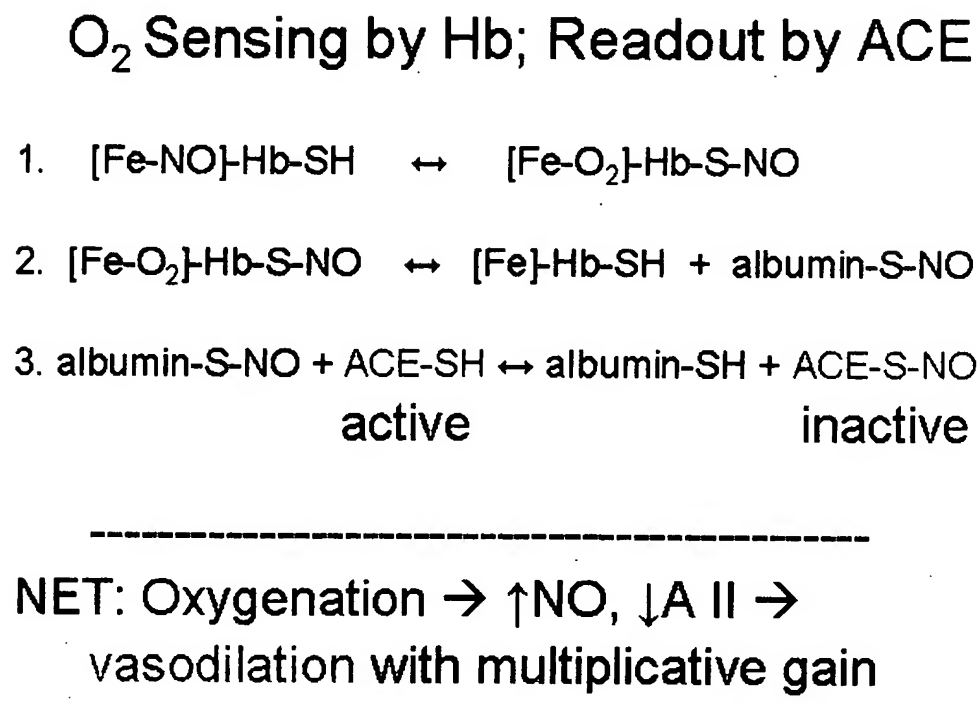


Figure 9. NO inactivation of sACE: possible sites of S-nitrosylation.

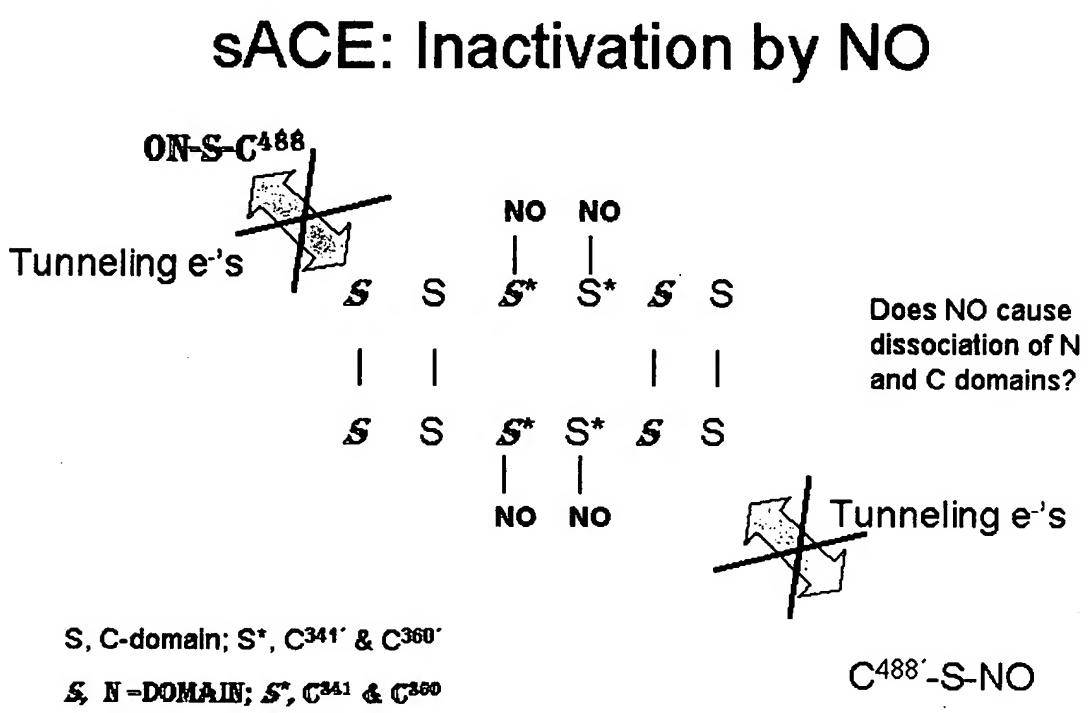


Figure 10. sACE on one immunocyte (T cell, monocyte/macrophage, or endothelial cell) binding to sACE on another immunocyte so as to promote specific cell-cell interactions. White triangle, "lid" formed by alpha helices α1 and α2; N and C, termini of each domain.

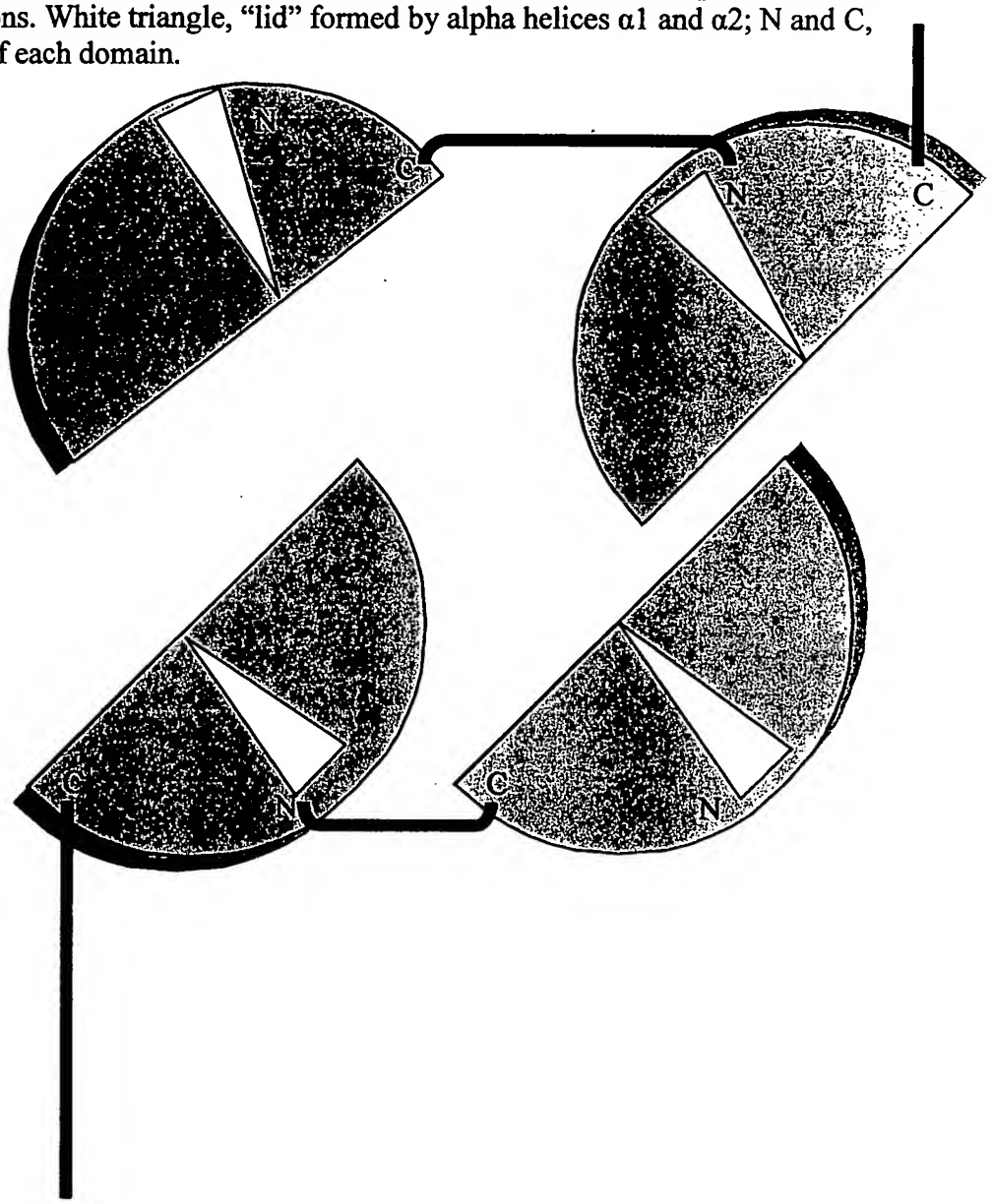
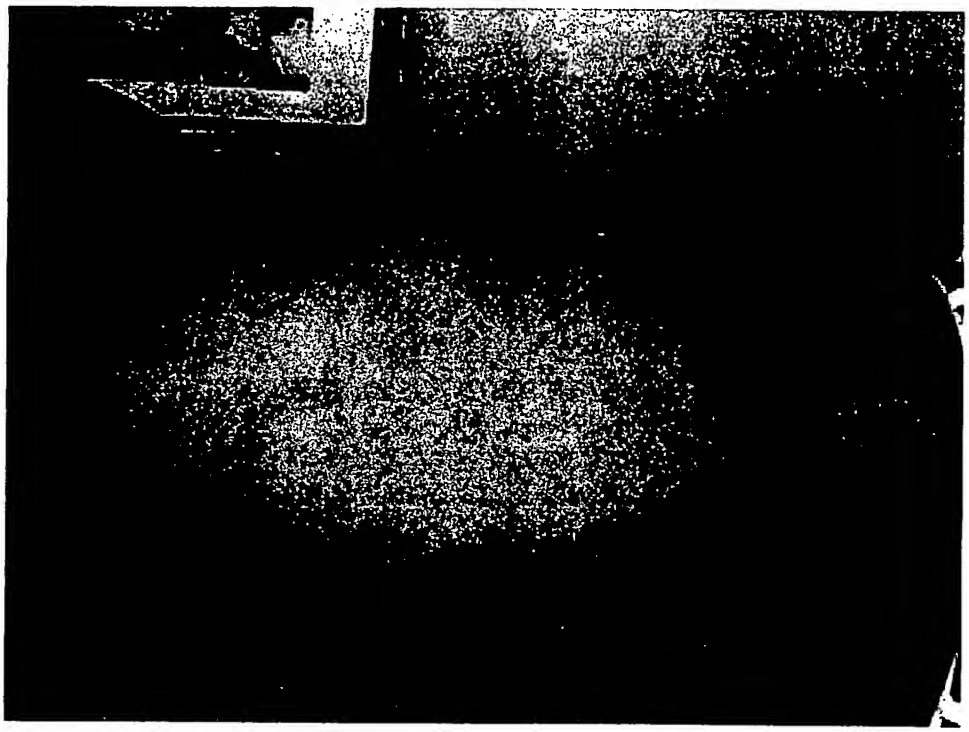


Figure 11. Prompt response to angiotensin II receptor blockade in a 33 yr old white man with psoriasis. a,b,c: back and nail before treatment; d,e,f: 3 weeks after taking valsartan 80 mg daily. In a second case, a 62 yr old white man with chronic psoriasis, for which he took 75 mg methotrexate daily, was able to stop his methtrexate within 2 months of starting quinapril 200 mg/day.

a



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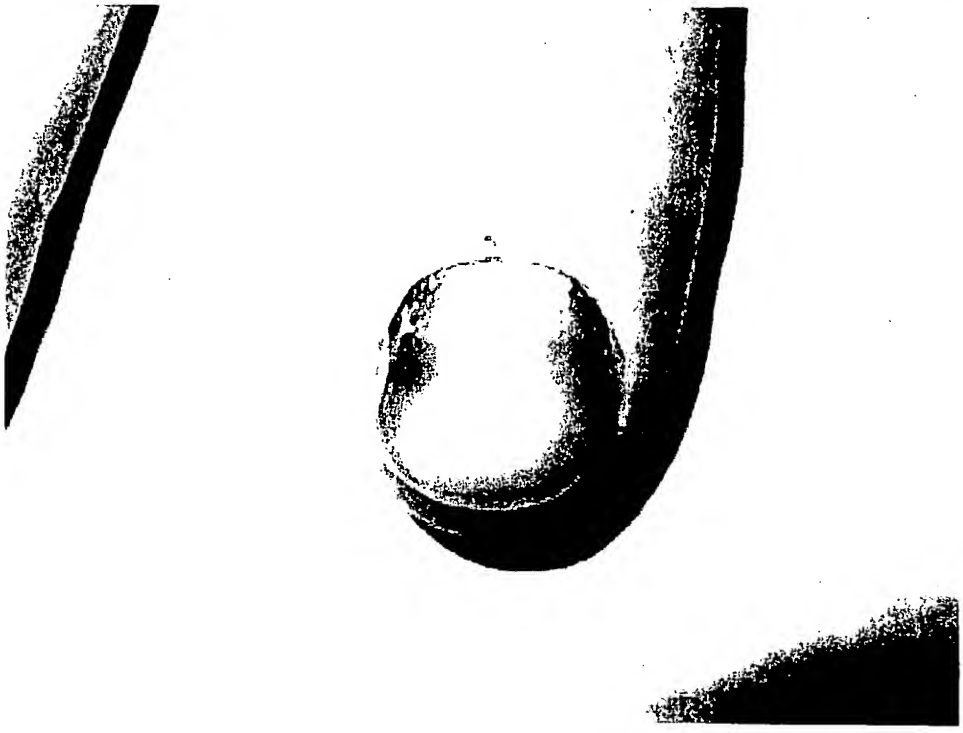

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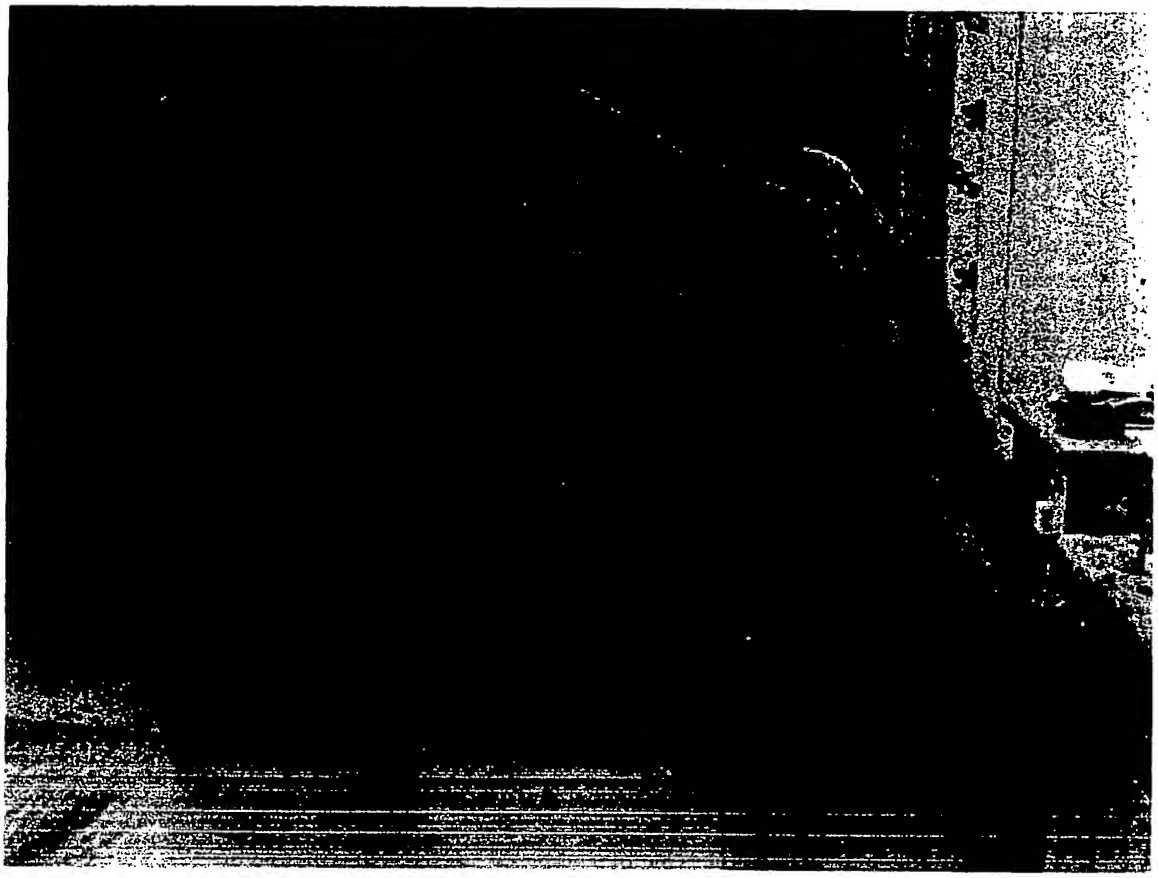

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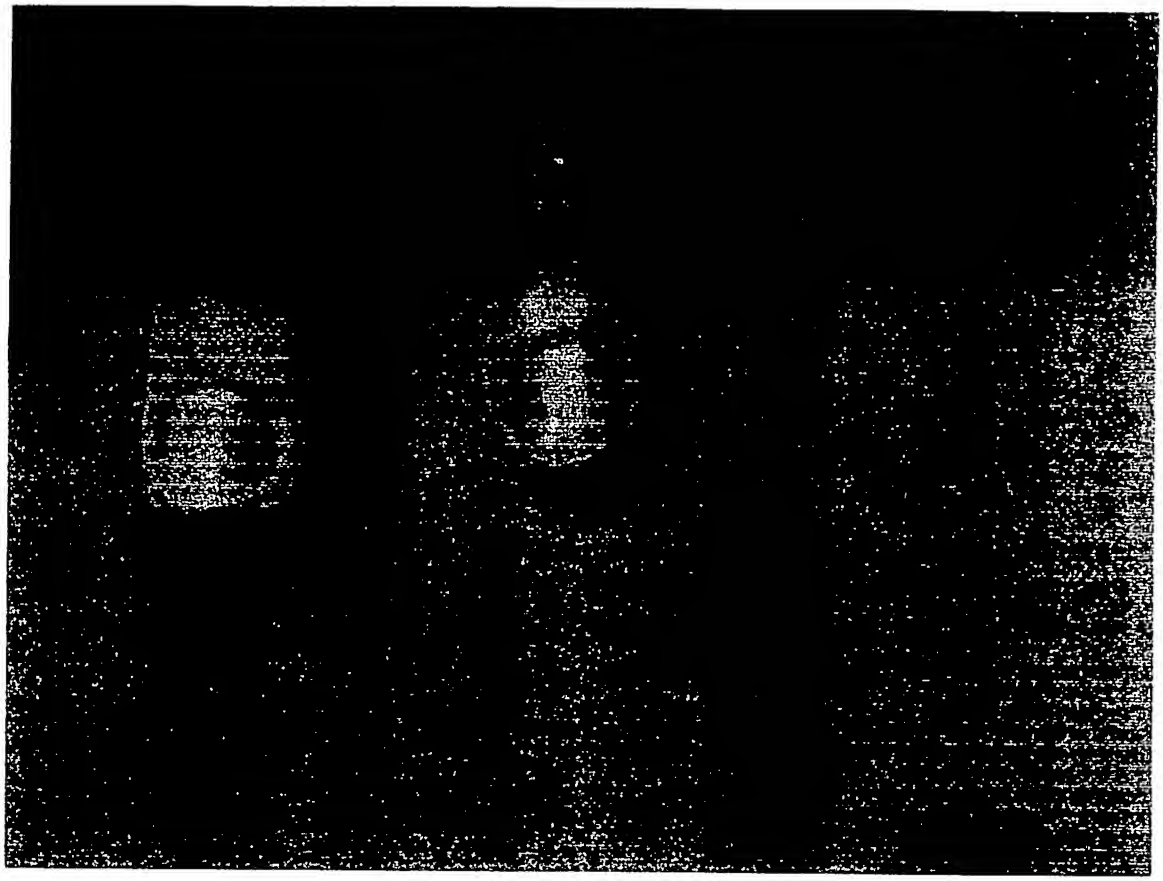

f

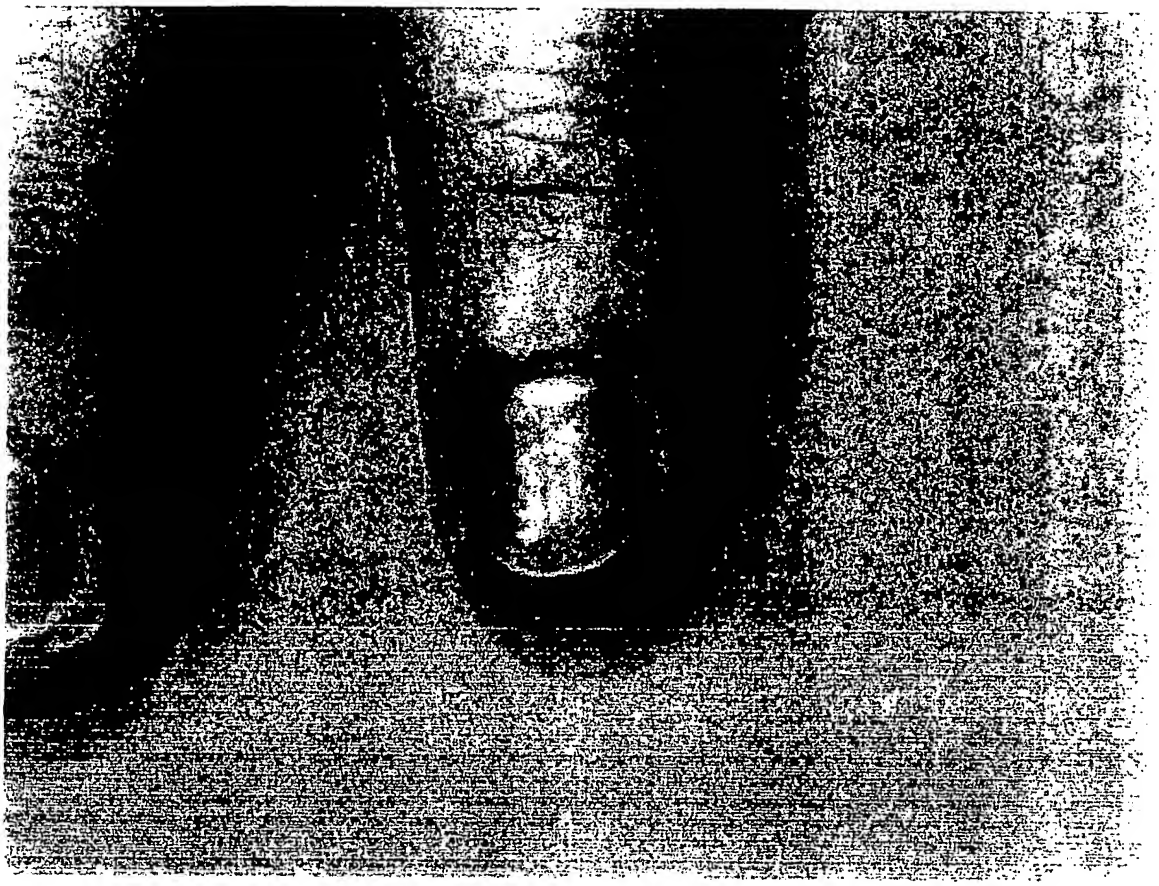

Figure 12. Genetic pathway for initiation of benign prostatic hyperplasia and prostate cancer. PDEF, prostate-derived ets factor.